REMARKS

The specification of the application has been amended to insert the generic names for RECIMADE® and ENBREL® (which are already referenced on page 99, lines 4 and 15 of the specification), correct the trademark names for RECIMADE® and ENBREL®, and delete a reference to an embedded hyperlink. The amendments to the specification do not constitute new matter.

Claims 1-71 were pending in this application. In view of their withdrawal from consideration, claims 2-5, 8-25, 32, 38, 41-61, 64, 65, 67, 68, 70 and 71 have been canceled, without prejudice. In order to expedite prosecution of the present application and without conceding to propriety of the rejections, Applicant has amended claims 6, 7, 26, 29, 31, 33-36, 39, 40, 63, 66 and 69 and canceled claims 1 and 37, without prejudice. Applicant reserves the right to pursue the subject matter of the canceled claims in a related application(s). New claims 72-75 have been added to more particularly point and distinctly claim that which Applicant regards as the invention. The claim amendments are fully supported by the specification of the present application as filed, *see e.g.*, page 21, lines 6-31; page 22, lines 9-20; page 41, lines 24-28; page 51, lines 11-32; page 59, lines 3-16; page 64, lines 27-32; page 84, line 22 to page 85, line 24; page 99, lines 3-8 and lines 14-26; page 137, line 31 to page 138, line 3; page 138, line 34 to page 139, line 9; page 150, lines 7-17 and page 152, lines 10-26 of the specification, and do not constitute new matter. Upon entry of the present amendments, claims 6, 7, 26-31, 33-36, 39, 40, 62, 63, 66, 67, 69 and 72-75 will be pending.

Applicant notes that a Supplemental Information Disclosure Statement and List of References Cited By Applicant accompanied by references B15-B23 and C01-C151 were filed by Express Mail in the United States Patent and Trademark Office on May 3, 2005. Applicant respectively requests that the Examiner enter and consider the references listed on the List of References Cited By Applicant filed on May 3, 2005 as well as the references listed on the List of References Cited by Applicant filed herewith.

Applicant respectfully requests consideration and entry of the amendments and remarks made herein into the record for the present application.

I. ENTITLEMENT TO PRIORITY

The Examiner has invited Applicant to verify the priority date of the pending claims. Applicant submits that support for pending claims 6, 7, 26-31, 33-36, 39, 40, 62, 63, 66, 67, 69 and 72-75 can be found in the three provisional applications that the present application

claims priority to under 35 U.S.C. § 119, namely U.S. provisional application Serial No. 60/273,098, filed March 2, 2001, U.S. application Serial No. 60/346,918, filed October 19, 2001, and U.S. provisional application Serial No 60/358,424, filed February 19, 2002.

II. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1, 6, 7, 26-31, 33-37, 39, 40, 62, 63, 66 and 69 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner contends that claims 1, 7, 30, 33, 40 and 63 and dependent claims thereof are indefinite because the recitation of MEDI-507, LFA3TIP, REMICADE® and/or ENBREL® do not clearly define the antibodies and fusion proteins. For the reasons detailed below, the rejection cannot stand and should be withdrawn.

In order to expedite prosecution of the present application and without conceding to the propriety of the rejection, Applicant has amended claim 63 to recite "infliximab" and "etanercept", which as evidenced by the enclosed product information from the Physicians Desk Reference, 55th edition, 2001 (a copy of which is enclosed as Exhibit A), are the generic names for REMICADE® and ENBREL®, respectively. Applicant also respectfully points out that the specification as filed references infliximab and etanercept as the generic names for REMICADE® and ENBREL®, respectively. *See* page 99, lines 4 and 15 of the specification of the present application. Applicant respectfully asserts that one of skill would have been able to ascertain the antibody and fusion protein encompassed by the terms "infliximab" and "etanercept."

Applicant respectfully asserts that one of skill in the art would have been able to ascertain the antibody and fusion protein encompassed by the terms "MEDI-507" and "LFA3TIP." The specification of the present application teaches that MEDI-507 is disclosed in International Publication No. WO 99/03502 ("Bazin") and U.S. application Serial No. 09/462,140 and incorporates these references into the specification. *See* page 64, lines 29-31 of the specification of the present application. Bazin, which has been cited as prior art by the Examiner, published on January 28, 1999, before the filing date of the present application, describes in Example 11 the construction and analysis of MEDI-507. Figures 31 and 42 of Bazin provide the amino acid sequences for the light chain variable region and heavy chain variable region of MEDI-507. Thus, Applicant submits that one of skill in the art would have been able to ascertain the antibody encompassed by the term "MEDI-507."

The specification of the present application teaches that LFA3TIP is available by Biogen, Inc. of Cambridge Massachusetts. U.S. Patent No. 6,162, 432 (the "'432 Patent"), which issued on December 19, 2000 and is assigned to Biogen, Inc. (Cambridge, MA) et al., provides the amino acid and nucleotide sequences for LFA3TIP (see SEQ ID NO:7 of the '432 Patent). The '432 Patent also states that the plasmid, pSAB152, encoding LFA3TIP was deposited with the ATCC under Accession No. 68720. Thus, Applicant respectfully submits that one of skill in the art would have been able to ascertain the fusion protein referred to as "LFA3TIP."

In view of the foregoing, Applicant respectfully asserts that the rejection under 35 U.S.C. § 112, second paragraph, cannot stand and should be withdrawn.

III. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1, 7, 30, 33, 40 and 63 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicant submits that the antibodies and fusion proteins referred to as "MEDI-507", "LFA3TIP", "REMICADE®", and "ENBREL®" were known and readily available to the public as of the effective filing date for the present application. As evidenced by the enclosed product information for REMICADE® (infliximab) and ENBREL® (etanercept), REMICADE® (infliximab) and ENBREL® (etanercept) were commercially available as of the effective date of the present application. As discussed above, the amino acid sequences for MEDI-507 and LFA3TIP were available to one of skill in the art as of the effective date of the present application. *See* Example 11 and Figures 31 and 42 of Bazin, and SEQ ID NO:7 of the '432 Patent. Techniques for producing MEDI-507 and LFA3TIP are described in the specification of the present application and were known to one of skill in the as of the effective date of the present application. *See*, *e.g.*, page 153, line 7 to page 169, line 2 of the specification of the present application. Thus, Applicant respectfully asserts that one of skill in the art would have been able to obtain or make the antibodies and fusion proteins referred to as "MEDI-507", "LFA3TIP", "REMICADE®", and "ENBREL®." Accordingly, Applicant submits that the specification of the present application fully enables one of skill in the art to practice the claimed methods.

In view of the foregoing, the rejection under 35 U.S.C. § 112, first paragraph, cannot stand and should be withdrawn.

IV. THE REJECTION UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN

Claims 1, 6, 7, 26-31, 33-37, 39, 40, 62, 63, 66 and 69 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bazin in view of the '432 Patent, Branco et al., 1999, Transplantation 68(10): 1588-1596 ("Branco"), Lee *et al.*, U.S. Patent No. 6,277,969 ("'969 Patent"), and Strom *et al.*, Therapeutic Immunology, Austen et al (eds), Blackwell Science, Cambridge, MA, 1996 at pages 451-456 ("Strom"). The Examiner contends that: (a) Bazin teaches a method of treating an autoimmune disorder or inflammatory disorder comprising administering to subject in need thereof a therapeutically effective amount of one or more CD2 binding molecules, such as anti-CD2 antibodies (*e.g.*, LO-CD2a and MEDI-507); (b) Bazin also teaches that LO-CD2a and MEDI-507 can be administered at an initial dose of 1 mg via intravenous infusion, and that anti-CD2 antibodies can be combined with other agents that inhibit the activation of T cells; (c) the '432 Patent teaches a method of treating an autoimmune disorder or inflammatory disorder, such as psorasis, comprising administering to a subject in need thereof a therapeutically effective amount of one or more CD2 binding molecules, such as an anti-CD2 antibody and LFA3TIP; (d) Branco teaches that MEDI-507 is begin investigated for use in autoimmune and other chronic inflammatory conditions such as psorasis and that it would be desirable to combine MEDI-507 with other biological agents having different modes of action; (e) the '969 Patent teaches the administration of anti-TNFα antibodies, such as cA2, to treat diseases related to angiogenesis such as psoriasis; and (f) Strom teaches that a multitiered approach to immunosuppressive therapy was known and practiced by the ordinary artisan. The Examiner concludes that one of skill in the art at the time of the invention would have been motivated and would have had a reasonable expectation of success for treating psorasis by administering multiple immunosuppressive agents, such as MEDI-507 and/or LFA3TIP, in conjunction with an anti-angiogenic factor, such as REMICADE®. For the reasons below, the rejection cannot stand and should be withdrawn.

A finding of obviousness requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1996). The proper inquiry is whether the art suggests the invention, and whether the art provides one of ordinary skill in the art with a

reasonable expectation of success. *In re O'Farrell* 853 F.2d 894, 7 U.S.P.Q. 2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Appellants' disclosure. *In re Vaeck* 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991).

None of the cited references, alone or in combination, teach or suggest treating an autoimmune disorder or an inflammatory disorder by administering to a subject in need thereof a therapeutically effective amount of one or more CD2 binding molecules, such as MEDI-507 and LFA3TIP, and a therapeutically effective amount of one or more anti-angiogenic agents.

Bazin does not teach what techniques, drugs or compounds may be employed to inhibit the activation of T-cells or inhibit graft rejection or graft versus host disease. Bazin merely states that anti-CD2 antibodies may be combined with other techniques, drugs or compounds that inhibit the activation of T-cells or inhibit graft rejection or graft versus host disease. *See* Bazin at page 20, lines 32-36. In the absence of any guidance from Bazin, one of ordinary skill in the art would have been left to select a technique, drug or compound that inhibits the activation of T-cells or inhibits graft rejection or graft versus host disease from a vast number of possibilities. It would not have been obvious to one of ordinary skill in the art to select the combination of a CD2 binding molecule, such as MEDI-507 or LFA3TIP, and an anti-angiogenic agent, such as REMICADE® or ENBREL®, for the treatment of an autoimmune disorder or an inflammatory disorder from the vast number of possible combinations.

The secondary references cited by the Examiner do not cure the deficiency of Bazin. The '432 Patent describes methods for treating skin conditions characterized by increased T cell activation and abnormal antigen presentation in the dermis and epidermis in mammals using inhibitors of the CD2/LFA3 interaction. The '432 Patent does not teach or suggest combining a CD2 binding molecule with an anti-angiogenic agent for the treatment of an autoimmune disorder or an inflammatory disorder. The '432 Patent states that an inhibitor of the CD2/LFA interaction may be administered in conjunction with other therapeutic or prophylactic agents and that these agents include cyclosporine A, steroids, retinoids, nitrogen mustard, interferon, methotrexate, antibiotics, antihistamines, chemotherapeutics, and PUVA. See the '432 Patent at col. 16, lines 39-43 and lines 54-57. Given the list of agents in the '432 Patent, it would not have been obvious to one of ordinary skill in the art to select the combination of a CD2 binding molecule, such as MEDI-507 or LFA3TIP, and an anti-

angiogenic agent, such as REMICADE® or ENBREL® for the treatment of an autoimmune disorder or an inflammatory disorder.

Branco describes the activity of MEDI-507 in various *in vitro* assays. Contrary to the Examiner's contention, Branco does not teach or suggest combining MEDI-507 with other biological or chemical agents with differing modes of action for the treatment of an autoimmune disorder or an inflammatory disorder. Rather, Branco suggests that it is possible that the "combination of MEDI-507 and other biological or chemical agents with differing modes of action could induce long-term tolerance to foreign tissue." *See* Branco at page 1595, right col., last sentence. Thus, Branco suggests that it might be possible to use a combination of MEDI-507 and other biological or chemical agents to inhibit graft rejection or graft versus host disease. Therefore, in view of the teaching in Branco, it would not have been obvious to one of ordinary skill in the art to select the combination of a CD2 binding molecule, such as MEDI-507 or LFA3TIP, and an anti-angiogenic agent, such as REMICADE® or ENBREL® for the treatment of an autoimmune disorder or an inflammatory disorder.

The '969 Patent describes anti-TNFα antibodies and anti-TNFα peptides, and the use of such antibodies and peptides to treat a large number of TNF-related pathologies. The '969 Patent does not teach or suggest combining an anti-TNFα antibody and a CD2 binding molecule for the treatment of an autoimmune disorder or an inflammatory disorder. The '969 Patent states that anti-TNFα antibodies and anti-TNFα peptides can be utilized in combination with TNF therapy to block undesired effects of TNF, and lymphokines, hematopoietic growth factors, and other monoclonal antibodies, chimeric antibodies, and murine antibodies which increase the number or activity of effector cells which interact with the antibodies. *See* the '969 Patent at col. 37, lines 47-55. Given the teaching in the '969 Patent, it would not have been obvious to one of ordinary skill in the art to select the combination of a CD2 binding molecule, such as MEDI-507 or LFA3TIP, and an anti-angiogenic agent, such as REMICADE® or ENBREL® for the treatment of an autoimmune disorder or an inflammatory disorder.

Strom is merely a review article that describes therapeutic approaches for organ transplant patients. There is no teaching or suggestion in Strom to treat an autoimmune disorder or an inflammatory disorder, much less any teaching or suggestion to treat such a disorder by administering to a subject in need thereof a CD2 binding molecule, such as MEDI-507 or LFA3TIP, and an anti-angiogenic agent, such as REMICADE® or ENBREL®.

Accordingly, the deficiency in Bazin is not cured by the four (4) secondary references cited by the Examiner.[1] The combination of Bazin and the secondary references do not teach or suggest the use of a CD2 binding molecule, such as MEDI-507 or LFA3TIP, and an anti-angiogenic agent, such as REMICADE® or ENBREL®, for the treatment of an autoimmune disorder or an inflammatory.

There is no suggestion or motivation to modify the cited references to administer the combination of a CD2 binding molecule and an anti-angiogenic agent to a subject in need thereof to treat an autoimmune disorder or an inflammatory disorder. The Examiner is improperly relying on hindsight reasoning obtained from the specification of the present application to arrive at the claimed invention. It is impermissible to engage in hindsight reasoning, using the claims as a frame and the prior art reference as a mosaic to piece together a facsimile of the claimed invention. *W.L. Gore & Assoc., Inc. v. Garlock, Inc.* 220 USPQ 303, 312 (Fed. Cir. 1983).

In view of the foregoing, the rejection under 35 U.S.C. § 103(a) cannot stand and should be withdrawn.

V. THE NON-STATUTORY OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION SHOULD BE HELD IN ABEYANCE

Claims 6, 7, 26-28, 31, 33-37, 39, 66, and 69 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as being unpatentable over claims 37-39 and 42-54 of copending U.S. application Serial No. 10/091,236. Applicant respectfully requests that this rejection be held in abeyance until such time as there is allowable subject matter. At such time, Applicant will consider whether the filing of a terminal disclaimer is warranted.

CONCLUSION

Applicant believes that the present claims meet all of the requirements for patentability. Entry and consideration of the foregoing amendments and remarks into the file of the present application is respectfully requested.

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[1] The Examiner's citation of a total of five references to reject the claims as obvious indicates the weakness of the Examiner's position.

If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicant's undersigned attorney invites the Examiner to telephone her at the number provided below.

Respectfully submitted,

Date: March 12 , 2007

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